REMARKS

Reconsideration and withdrawal of the rejections of the present application are respectfully requested in view of the amendments to the claims and specification, as well as the remarks presented herewith, which place the application into condition for allowance.

Status of the Claims and Formal Matters

Claims 16-27 are pending in this application. By this paper, Claims 1 and 7 have been cancelled, without prejudice and Claims 16-27 have been added. Support for the amended recitations can be found in the cancelled claims and throughout the specification. In particular, the new recitations find support *inter alia* at page 1, lines 15-27, page 5, lines 1-3, page 1, lines 6-10, page 6, lines 20 and 21, page 1, lines 14 and 15, page 7, lines 12-19, page 7, lines 5-6, page 12, lines 15-16, page 9, lines 11-12, page 22, lines 26-28, page 11, lines 19-20, page 11, lines 22-26 of the application as filed. No new matter has been introduced by this amendment.

Specification

The Examiner has objected to the disclosure because the polypeptide sequences must be identified by sequence identifiers. Applicants amended the specification at pages 30 and 31 to insert appropriate sequence identifiers. Accordingly, Applicants request reconsideration and withdrawal of the objection.

The Examiner has objected to the title of the invention as being allegedly not descriptive. In view of the amendments to the title, Applicants request reconsideration and withdrawal of the objections.

Rejections.

Rejection under 35 U.S.C. § 112.

Claims 1-7 were rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of cancellation of claims 1-7, Applicants request withdrawal and reconsideration of the rejection. New claims 16-27 are fully compliant with the requirements of the 35 U.S.C. §112, second paragraph.

Rejections under 35 U.S.C. §102(e)

Claims 1-7 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Kornbluth et al., US 20020188104 "Kornbluth" as allegedly evidenced by Shisheva, Methods in Enzymology, (2001), Vol. 329, 39-50,"Shisheva", Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, "Leung" or Zarsky et al., FEBS Letters (1997), vol. 403, 303-308, "Zarsky". The Office Action contends that Kornbluth allegedly discloses arrays containing isolated cytosol, which would inherently comprise cytosolic accessory proteins as evidenced by Shisheva, Leung or Zarsky. This rejection is respectfully traversed in view of the cancellation of claims 1-7. Further, Applicants submit that in view of the remarks presented herewith, new claims 16-27 are not anticipated by Kornbluth as evidenced by Shiseva, Leung or Zarsky.

The invention relates *inter alia* to an array comprising a surface having attached thereto at least one cytosolic accessory protein of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins, wherein said cytosolic accessory protein is free from membrane protein components or other subunits of said ion channel, G protein coupled receptor or transmembrane transporter protein complex.

At best, Kornbluth relates to a human homolog of *Drosophila melanogaster* Reaper (Rpr) protein and nucleic acid sequences, antisense nucleic acid sequences thereto, antibodies specific to human Reaper protein (hRpr) and methods of screening for modulators of hRpr activity. Further, contrary to the Examiner's allegations, the function-based assays disclosed in Kornbluth involve arrays of mitochondria from X*enopus* extracts, which are "probed" with isolated cytosol or cytosol depleted immunodepleted of the hRpr interacting protein Scythe. Alternatively, the arrays of mitochondria as disclosed in Kornbluth can be probed by addition of hRpr and test compounds.

Thus, in contrast to the new claim 16, Kornbluth does not teach an array comprising a surface having attached thereto at least one cytosolic accessory protein of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins, wherein said cytosolic accessory protein is free from membrane protein components or other subunits of said ion channel, G protein coupled receptor or transmembrane transporter protein complex.

Due to these deficiencies, Kornbluth fails to anticipate an instant array of cytosolic proteins. Under §102, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Consequently, Applicants assert that a §102(e) rejection in view of Kornbluth is moot.

The Examiner further contends that protein array of Kornbluth would allegedly comprise accessory proteins to membrane proteins as allegedly evidenced by Shisheva, Leung and Zarksy. Applicants respectfully disagree. Anticipation by inherency requires that the prior art reference disclose each and every limitation of the claim. *Standard Havens Prods., v Gencor Indus., Inc.*, 953 F.2d 1360, 1369 (Fed. Cir. 1991). At best, Shisheva relates to GDP (guanidine nucleotide diphosphate) dissociation inhibitor (GDI) proteins that form stable complexes with GDP-loaded prenylated Rab. The GDI's are involved in cellular trafficking of Rab, transporting GDP bound-Rab to membranes and retrieving inactivated Rab and returning them to their membrane of origin. Three mammalian GDI genes are mentioned, which encode ubiquitously expressed highly homologous protein isoforms. Rabs are mentioned to be hydrophobic peripheral membrane proteins (page 40, lines 2–3).

Applicants respectfully point out that Rabs are members of the Ras super family of G proteins and thus are not ion channels, G protein coupled receptors or transmembrane transporter proteins. Thus, GDI proteins discussed by Shisheva are not cytosolic accessory proteins of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins. Thus, Shisheva does not anticipate arrays of cytosolic accessory proteins.

Further, Leung does not anticipate arrays of cytosolic accessory proteins. At best, Leung relates to a cytosolic protein p16 that co purifies with the heat shock protein Hsc70. Hsc70 is described as being a cytoplasmic protein, from the abstract: "Cytoplasmic HSC70 is a multifunctional molecular chaperone" and "p16 may be a unique Nm23/NDP kinase that functions as an accessory protein for cytosolic Hsc70 in eukaryotes". Thus, p16 is clearly not

considered to be a "cytosolic accessory protein of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins".

Finally, Zarsky relates to cloning of a Rab GDI from the plant *Arabidopsis thaliana.*

However, Rab GDI proteins are not cytosolic accessory proteins of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins. Thus, Zarsky does not anticipate arrays of cytosolic accessory proteins.

In view of the arguments above, Applicants request withdrawal and reconsideration of the rejection under 35 U.S.C.§102(e) over Kornbluth.

Rejections under 35 U.S.C. §102(e)

Claims 1-7 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Charych et al., US 2002055125 "Charych" as allegedly evidenced by Shisheva, Methods in Enzymology, (2001), Vol. 329, 39-50,"Shisheva", Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614,"Leung" or Zarsky et al., FEBS Letters (1997), vol. 403, 303-308, "Zarsky". The Office Action contends that Charych allegedly discloses arrays of samples derived from cytosol, which would inherently comprise cytosolic accessory proteins as evidenced by Shisheva, Leung or Zarsky. This rejection is respectfully traversed in view of the cancellation of claims 1-7. Further, Applicants submit that in view of the remarks presented herewith, new claims 16-27 are not anticipated by Charych as allegedly evidenced by Shiseva, Leung or Zarsky.

At best, Charych relates peptidomimetic protein-binding arrays. The protein-binding array elements of Charych include a peptidomimetic segment linked to a solid support via a stable anchor. Charych defines "peptidomimetic arrays" at page 3, paragraph 0034 as follows:

"Peptidomimetic arrays in accordance with the present invention are composed of a number of different array elements comprising protein-binding agents attached to the surface of a solid support. The different protein-binding agent array elements each include an anchoring segment attached to the substrate surface, a peptidomimetic protein-binding segment, and a linker segment connecting and separating the anchoring and peptidomimetic segments. A "peptidomimetic" as used herein refers to nonpeptide synthetic polymers or oligomers that

detectably interact with proteins or receptors in a manner analogous to protein-protein or protein-peptide physical and/or chemical interactions under assay conditions."

Charych provides a further description of peptidomimetics at paragraphs 0057 and 0059 as follows:

"A "peptidomimetic" as used herein refers to nonpeptide synthetic polymers or oligomers that detectably interact with proteins or receptors in a manner analogous to protein-protein or protein-peptide physical chemical interactions under assay conditions. ...."

Further, Charych states: "In a preferred embodiment of the present invention, the peptidomimetic segment of the protein-binding agent is a peptoid. The term "peptoid" as used herein refers to polymers comprising N^{α}-substituted amides..." Based on the above cited disclosure, it is clear that entities immobilized on arrays taught by Charych are peptidomimetics, such as nonpeptide synthetic polymers or oligomers. Thus, Charych does not describe arrays of cytosolic accessory proteins.

Due to these deficiencies, Charych fails to anticipate an instant array of cytosolic proteins. Under §102, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Consequently, Applicants assert that a §102(e) rejection in view of Charych is moot. Furthermore, in view of the remarks above, protein array of Charych does not comprise accessory proteins to membrane proteins as allegedly evidenced by Shisheva, Leung and Zarksy. Reconsideration and withdrawal of the rejection is hereby respectfully requested.

Rejections under 35 U.S.C. §102(b)

Claims 1-7 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Patron et al., US 20010041349 "Patron" as allegedly evidenced by Shisheva, Methods in Enzymology, (2001), Vol. 329, 39-50,"Shisheva", Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614,"Leung" or Zarsky et al., FEBS Letters (1997), vol. 403, 303-308, "Zarsky". The Office Action contends that Patron allegedly discloses arrays of recombinant proteins, which would inherently comprise cytosolic accessory proteins as allegedly evidenced by

Shisheva, Leung or Zarsky. This rejection is respectfully traversed in view of the cancellation of claims 1-7. Further, Applicants submit that in view of the remarks presented herewith, new claims 16-27 are not anticipated by Patron as allegedly evidenced by Shiseva, Leung or Zarsky.

At best, Patron relates to an array of protein expression systems comprising: (a) a substrate; (b) a binding surface which covers some or all of the substrate surface; and (c) a plurality of protein expression systems located at discrete positions on portions of the substrate covered by the binding surface. Patron does not teach an arrays of cytosolic accessory proteins of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins, wherein said cytosolic accessory protein is free from membrane protein components or other subunits of said ion channel, G protein coupled receptor or transmembrane transporter protein complex.

The Examiner has cited paragraph 20 as support for his argument that Patron teaches immobilized proteins wherein the proteins are of the same family and wherein the family includes intracellular signal transduction modulators and effectors apoptosis related factors and other factors reading on accessory proteins. Applicants respectfully point out that cited embodiment relates to arrays of immobilized protein expression systems, and not to the immobilized proteins *per se*. Furthermore although cytosolic accessory proteins can be intracellular signal transduction modulators and effectors or apoptosis factors, not all signal transduction modulators and effectors or apoptosis factors are cytosolic accessory proteins. The terms intracellular signal transduction modulators and effectors or apoptosis factors are not co-terminous with cytosolic accessory proteins.

Due to these deficiencies, Patron fails to anticipate an instant array of cytosolic proteins. Under §102, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Consequently, Applicants assert that a §102(e) rejection in view of Patron is moot. Furthermore, in view of the remarks above, protein array of Patron does not comprise accessory proteins to membrane proteins as evidenced by Shisheva, Leung and Zarksy. Reconsideration and withdrawal of the rejection is hereby respectfully requested.

Rejections under 35 U.S.C. §102(b)

Claims 1-7 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wagner et al., WO 0004382 "Wagner" as allegedly evidenced by Shisheva, Methods in Enzymology, (2001), Vol. 329, 39-50,"Shisheva", Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614,"Leung" or Zarsky et al., FEBS Letters (1997), vol. 403, 303-308, "Zarsky". The Office Action contends that Wagner allegedly discloses arrays of proteins which would inherently comprise cytosolic accessory proteins as allegedly evidenced by Shisheva, Leung or Zarsky. This rejection is respectfully traversed in view of the cancellation of claims 1-7. Further, Applicants submit that in view of the remarks presented herewith, new claims 16-27 are not anticipated by Wagner as evidenced by Shiseva, Leung or Zarsky.

At best, Wagner relates to an array of proteins and methods for the parallel in *vitro* screening of plurality of protein-analyte interactions. In Example 9, Wagner describes experiments wherein cleared cell lysate is bound to an array of immobilized scFv fragments. The proteins bound to the scFv array are not further characterized or described. Further in Example 10, Wagner describes experiments wherein cleared cell lysate is bound to an array of immobilized monoclonal antibody; the bound proteins are not further characterized or described.

As mentioned above, cytosolic accessory proteins can be intracellular signal transduction modulators and effectors or apoptosis-related factors, not all signal transduction modulators and effectors or apoptosis factors are cytosolic accessory proteins. The terms intracellular signal transduction modulators and effectors or apoptosis-related factors are not co-terminous with cytosolic accessory proteins. Thus, Wagner does not disclose an array of cytosolic accessory proteins of a membrane protein selected from ion channels, G protein coupled receptors and transmembrane transporter proteins, wherein said cytosolic accessory protein is free from membrane protein components or other subunits of said ion channel, G protein coupled receptor or transmembrane transporter protein complex.

Due to these deficiencies, Wagner fails to anticipate an instant array of cytosolic proteins. Under §102, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Consequently, Applicants assert that a §102(e) rejection in view of Wagner is moot. Furthermore, in view of the remarks above, protein array of Wagner does not comprise accessory proteins to membrane proteins as allegedly evidenced by Shisheva, Leung and Zarksy. Reconsideration and withdrawal of the rejection is hereby respectfully requested.

CONCLUSION

Favorable action on the merits is respectfully requested. If any discussion regarding this Response is desired, the Examiner is respectfully urged to contact the undersigned at the number given below, and is assured of full cooperation in progressing the application to allowance.

Applicants believe no fees are due with the filing of this Response. However, if any additional fees are required or if any funds are due, the USPTO is authorized to charge or credit Deposit Account Number: **50-0311**, Customer Number: **35437**, Reference Number: **33694-508001US**.

Respectfully submitted,

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